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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/599,567	10/02/2006	Julia Greil	33704-US-PCT	1912

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EXAMINER	
SOROUSH, ALI	
ART UNIT	PAPER NUMBER
1616	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/599,567	GREIL ET AL.	
	Examiner	Art Unit	
	ALI SOROUSH	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16,18 and 20-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16,18 and 20-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *04132007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

Through a preliminary amendment filed on 10/02/2006, claims 9, 10, 18 and 21 are currently amended and claims 17, 19, and 23-24 are cancelled. Therefore, claims 1-16, 18, and 20-22 are currently pending examination for patentability.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise and exact terms as to enable any : person skilled in the ad to which it pertains, or with which It is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 18 is rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for prophylaxis of diabetes mellitus. The claim contains subject matter was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. While the specification is enabled for the treatment of diabetes mellitus, it does not provide sufficient information that diabetes mellitus can be prevented with the composition instantly claimed.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to In re Wands, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing Ex parte Forman, 230 USPQ 546 (BdApIs 1986) at 547 the court recited eight factors:

(1) the nature of the invention, (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims', (6) the amount of direction or guidance presented', (7) the presence or absence of working examples', and (8) the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

(1). The Nature of the Invention: the rejected claim 18 is drawn to, “a coprecipitate of amorphous maleate with a pharmaceutically acceptable carrier according to claim 1, for use in the treatment and/or prophylaxis of diabetes mellitus …”

(2). The state of the prior art: In the instant case, the specification does not provide guidance as to how one skilled in the art would accomplish the objective of **prophylaxis of** diabetes mellitus. The state of the art for prevention of diabetes mellitus is low.

(3). The predictability or unpredictability of the art: the art does not enable a person of ordinary skill in the art to make and use the claimed invention without resorting to undue experimentation.

The specification fails to enable one of ordinary skill in the art to practice the presently claimed method for preventing diabetes mellitus. The term "prevention" or "preventing" is synonymous with the term "curing" and both circumscribe methods of treatment having absolute success. Since absolute success is not as of yet reasonably possible with most diseases/disorders, the specification is viewed as lacking an adequate enablement of where diabetes mellitus may be actually prevented.

(4). The breadth of the claims: the claims encompass co-precipitate of rosiglitazone maleate for use in prophylaxis of diabetes mellitus. Applicant fails to set forth the criteria that define the preventing of the disease. Thus, the breadth of the claim is over broad.

(5). The amount of direction or guidance presented: does not provide any guidance in terms of preventing diabetes mellitus.

(6). The presence or absence of working examples: while applicant is enabled for the treatment diabetes mellitus, applicant does not provide any working examples for the preventing diabetes mellitus. The applicant has not provided any competent evidence or disclosed any tests that are highly predictive for the preventative effects of the instant composition.

(7). The quantity of experimentation necessary: the quantity of experimentation would be an undue burden to one of ordinary skill in the art and amount to the trial and error type of experimentation. Thus, factors such as "sufficient working examples, "the level of skill in the art' and "predictability" etc. have been demonstrated to be sufficiently lacking in the instant case for the instant method claims.

In view of the breadth of the claims, unpredictability of preventing diabetes mellitus, and the lack of working examples regarding the activity as claimed, one skilled in the art would have to undergo an undue amount of experimentation to use the instantly claimed invention commensurate in scope with the claims.

The burden of enabling one skilled in the art to **preventing** diabetes mellitus would be much greater than that enabling the treatment. In the instant case, the specification does not provide guidance as to how one skilled in the art would accomplish the objective of preventing diabetes mellitus. Nor is there any guidance provided as to a specific protocol to be utilized in order to show the efficacy of the presently claimed composition for preventing diabetes mellitus.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 18 provides for the use of "in the treatment and/or prophylaxis of …", but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim 18 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 2, 7, 9-12, 14, 15, and 18 are rejected under 35 U.S.C. 102(e) as being anticipated by Ignatious et al. (US Patent Application 2006/0083784 A1, Published 04/20/2006).

Ignatious et al. teach in preferred example the preparation of a 1:2 wt:wt rosiglitazone maleate/methyl cellulose solid dispersion. “Rosiglitazone maleate (5g) was added to methyl cellulose (10g) in a mixture of methanol (200ml) and water (100ml). The mixture was stirred at ambient temperature until the solid is dissolved. The slightly cloudy solution was spray-dried using Niro SDMicro ..." (See paragraph 0019). Ignatious et al. teach that by this method an amorphous form of rosiglitazone maleate is prepared. (See paragraph 0043). Pharmaceutically acceptable carrier include methyl cellulose, polyvinylpyrrolidone, polyethylene glycol, and lactose. (See paragraph 0033). Organic solvents can be selected from methanol, ethanol, and acetone. (See paragraph 0055). With regard to the claim limitation of claim 18 reciting "for use in the treatment and /or prophylaxis of ...", this is an intended use and not given patentable weight in a product claim. For the foregoing reasons the instant claims are anticipated by the prior art.

Claims 1, 2, 3, 9-12, 16, and 18 rejected under 35 U.S.C. 102(e) as being anticipated by Boehm et al. (US Patent Application 2005/0163842 A1, Published 07/28/2005).

Boehm et al. teach in a preferred example the preparation of amorphous rosiglitazone. 8g of polyvinylpyrrolidone and 5.01g rosiglitazone free base is added to purified water, and then 13.6ml of maleic acid is added. A portion of the solution is then spray-dried to obtain an amorphous rosiglitazone maleate. (See paragraph 0327). In a second preferred embodiment 28g of polyvinylpyrrolidone and 28g rosiglitazone maleate are added to 325g of purified water. The solution is then spray-dried onto dibasic calcium phosphate dihydrate producing amorphous rosiglitazone maleate. (See paragraph 0329). Other suitable pharmaceutically acceptable polymeric carriers include methyl cellulose, polyvinylpyrrolidone, and gamma-cylcodextrins. (See paragraph 0265). The core (polymeric carrier and rosiglitazone maleate) can further include mannitol, lactose, and silicone dioxide. (See paragraph 188). With regard to the claim limitation of claim 18 reciting "for use in the treatment and /or prophylaxis of ...", this is an intended use and not given patentable weight in a product claim. For the foregoing reasons the instant claims are anticipated by the prior art.

Claims 20 and 22 are rejected under 35 U.S.C. 102(e) as being anticipated by Reddy et al. (US Patent Application 2004/0242658, Published 12/2/2004).

Reddy et al. teach a method of forming a pharmaceutical tablet of amorphous rosiglatazone. Where the active ingredient is brought into association with a carrier such

as polyethylene glycol 3000. (See title and paragraph 0038). For the foregoing reasons the instant claims are anticipated by the prior art.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Applicant Claims
2. Determining the scope and contents of the prior art.
3. Ascertaining the differences between the prior art and the claims at issue; and resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

1. Claims 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ignatious et al. (US Patent Application 2006/0083784 A1, Published 04/20/2006).

Applicant Claims

Applicant claims a method of preparing a co-precipitate of amorphous rosiglitazone maleate with a pharmaceutically acceptable carrier comprising the steps of dissolving rosiglitazone maleate in ethanol or acetone, adding the carrier, and spray-drying the solution.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

The teachings of Ignatious et al. is disclosed above.

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

Ignatious et al. does not anticipate where the method utilizes either ethanol or acetone as the organic solvent. However, Ignatious et al. does make such a method obvious.

Finding of Prima Facie Obviousness Rational and Motivation (MPEP §2142-2143)

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to use either ethanol or acetone instead of methanol in the method taught by Ignatious et al. One would have been motivated to do so because Ignatius teach all three as organic solvents and therefore they are suitable alternatives to each other. For the foregoing reasons the instant invention would have been obvious to one of ordinary skill in the art at the time of the instant invention.

2. Claims 4, 5, 6, 7, and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boehm et al. (US Patent Application 2005/0163842 A1, Published 07/28/2005).

Applicant Claims

Applicant claims a co-precipitate comprising amorphous rosiglitazone meleate and a pharmaceutical carrier selected from silicone dioxide, mannitol, lactose, methyl cellulose, and gamma-cyclodextrin.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

The teachings of Boehm et al. is disclosed above.

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

Boehm et al. does not anticipate a co-precipitate wherein the carrier is silicone dioxide, mannitol, lactose, methyl cellulose, or gamma-cyclodextrin. However, Boehm et al. does make such a co-precipitate obvious.

Finding of Prima Facie Obviousness Rational and Motivation (MPEP §2142-2143)

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to use either silicone dioxide, mannitol, lactose, methyl cellulose, or gamma-cyclodextrin instead of polyvinylpyrrolidone in the co-precipitate taught by Boehm et al. One would have been motivated to do so because Boehm et al. teach them all as carriers and therefore they are suitable alternatives to each other. For the foregoing reasons the instant invention would have been obvious to one of ordinary skill in the art at the time of the instant invention.

3. Claim 21 is rejected under 35 U.S.C. 103(a) as being unpatentable over Reddy et al. (US Patent Application 2004/0242658, Published 12/2/2004).

Applicant Claims

Applicant claims a solid solution of rosiglitazone maleate with polyethylene glycol.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

The teachings of Reddy et al. is disclosed above.

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

Reddy et al. does not anticipate a solid solution of rosiglitazone with polyethylene glycol. However, Reddy et al. does make such a solid solution obvious.

Finding of Prima Facie Obviousness Rational and Motivation (MPEP §2142-2143)

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to use polyethylene glycol in the solid solution taught by Reddy et al. One would have been motivated to do so because Reddy et al. teach that polyethylene glycol is suitable carrier for formulation for oral tablets of rosiglitazone maleate. For the foregoing reasons the instant invention would have been obvious to one of ordinary skill in the art at the time of the instant invention.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ali Soroush whose telephone number is (571) 272-9925. The examiner can normally be reached on Monday through Thursday 8:30am to 5:00pm E.S.T.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisor, Johann Richter can be reached on (571) 272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Ali Soroush
Patent Examiner
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/Mina Haghighatian/
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